REMARKS/ARGUMENTS

1. Claims 3-21 were previously pending. Claims 3-21 were rejected by the Office Action dated June 16, 2004. Claim 21 has been amended.

It is believed that this amendment places the application in condition for allowance.

2. Amended Claims:

Support for the claims previously presented in the Response of November 26, 2003, and Claim 21 as currently amended can be found in the specification as filed. Specifically, support for the claims is found at least in the Example 2, Tables 2; Example 3, Tables 3, 4, 5, and 7; Example 4, Table 9; Example 5, Table 10.

The amended claim, Claim 21 is set forth to claim a composition set forth in the application. Amended Claim 21 is drawn to the elected invention. Claim 21 recites a composition which has protectant and/or eradicant activity and which substantially inhibits bacterial and fungal growth, comprising a chitosan salt and an essential oil in a synergistically effective amount wherein the chitosan salt is present in an amount which is not inhibitory in the absence of the essential oil, wherein the concentration of the chitosan salt is in the range of 0.0016 - 0.1% (v/v), and wherein the essential oil is present in an amount which is not inhibitory in the absence of the chitosan salt, wherein the concentration of the essential oil is in the range of 0.025 - 0.1% (v/v). No new matter has been introduced by amendment.

Applicants hereby request further examination and reconsideration of the application, in view of the amendments and remarks.

4. • Claims 3-21 have been rejected under 35 U.S.C. 112, first paragraph.
• Claims 3-21 have been rejected under 35 U.S.C. 103(a).

Rejection of Claims under 35 U.S.C.112, first paragraph

5. The Examiner has rejected Claims 3-21 under 35 U.S.C. 112, first paragraph, for containing New Matter, and being based on a non-enabling specification.

The Examiner states in the Office Action mailed June 16, 2004, that (1) "[A]lmost the entire phrasing of new claim 21 appears to be New Matter. That is, reciting that both the chitosan salt and the essential oil are present in amounts which are not 'inhibitory' in the absence of the other appears to be New Matter, not supported by the specification. Also, the ranges .0016-.1% for the chitosan salt and .025 - .1% essential oil appear to be New Matter, not supported by the specification." The Examiner continues, (2) "Applicant's response filed December 1, 2003 makes brief reference to the specification for support for these recitations, but it is not clear to the examiner that these references support the recitation. To overcome the rejection, it would appear that a more detailed analysis of the specification is necessary since, on its face, there is no specific reference in the specification for neither component being in a concentration that is 'not inhibitory' by itself but synergistic together, nor are the ranges clearly disclosed." The Examiner further states (3) [N]ote, too, the phrase 'not inhibitory' is not seen to be clearly defined. Does this mean that in the concentration of the component would have

no antibacterial or antifungal ability at all? Clarification and/or correction is required". Finally, the Examiner states that "claim 21 recites 'preferably' in regard to the two ranges. 'Preferably', like the phrase 'such as' can be treated as an alternative recitation. That is, A preferably B can be construed as just A".

Applicant respectfully traverses the rejection. Matter that is added that makes explicit that which was implicit, inherent or intrinsic in the original disclosure is not new matter and is permitted. Further, with regard to the ranges recited in the claims, it is stated in the MPEP (MPEP 2163.05) that with regard to New Matter "the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. In the decision in *In re Wertheim*, 541 F2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of '25% -60%' and specific examples of '36%' and '50%'. A corresponding new claim limitation to 'at least 35%' did not meet the description requirement because the phrase 'at least' had no upper limit and caused the claim to read literally on embodiments outside the '25% to 60%' range, however, a limitation to "between 35% and 60%' did meet the description requirement".

In the instant case, Claim 21 (currently amended) recites a "composition which has protectant and/or eradicant activity and which substantially inhibits bacterial and fungal growth, comprising a chitosan salt and an essential oil in a synergistically effective amount wherein the chitosan salt is present in an amount which is not inhibitory in the absence of the essential oil, wherein the concentration of the chitosan salt is in the range of 0.0016 - 0.1% (v/v), and wherein the essential oil is present in an amount which is not inhibitory in the absence of the chitosan salt, wherein the concentration of the essential oil is in the range of 0.025 - 0.1% (v/v)."

To clarify, the phrase "not inhibitory" means that a particular concentration of the component has no antibacterial or antifungal ability at all, *i.e.*, there is 0% inhibition or colony growth is not inhibited.

With regard to the recitations of "the concentration of the chitosan salt is in the range of 0.0016 - 0.1% (v/v)" and "the concentration of the essential oil is in the range of 0.025 - 0.1% (v/v", the Examiner has indicated that "a more detailed analysis of the specification is necessary."

The specification discloses, "[A]s used herein, the term "synergism" is intended to include both an increased spectrum of activity (*i.e.*, greater activity against a broad spectrum of microorganisms), and/or increased efficacy (*i.e.*, greater activity against specific organisms than that predicted by use of either agent alone). The increased antimicrobial and antifungal activity of the synergistic combination permits **the use of smaller amounts of each agent thereby decreasing costs and minimizing other problems, *e.g.*, toxicity, solubility, availability.** Effectiveness against a broad spectrum of microorganisms broadens the utility of the synergistic product based on its effectiveness in environments containing many and diverse microorganisms which must be controlled" (Page 6, Lines 8-15). The specification also discloses that it "it is an object of the invention to provide a composition of natural compounds that act synergistically and are effective against postharvest pathogens and foodborne pathogens found on fruits and vegetables" (Page 4, Lines 1-3); that the present invention provides combinations of chitosan salts and essential oils that act synergistically both to protect food products from bacterial and fungal contamination and to eradicate or at least inhibit growth and toxin production in foods contaminated with bacteria and fungi (Paragraph bridging Pages 4 and 5); and that "[D]evelopment of

synergistic combinations of natural compounds can add a new dimension to their use as food preservatives, enhancing their effectiveness for stability, low toxicity, availability, and broad utility (Page 3, Lines 20-22).

Thus, Applicants have indicated that it is an object of the invention to use smaller amounts of chitosan salts and essential oils that act synergistically. Undue experimentation would not be required to determine that concentration range of individual reagents or combinations that do or do not inhibit in a given situation; determination of the required dose to obtain a desired response is common practice in the art.

Thus, the specification teaches that particular concentrations of chitosan acetate, chitosan propionate, and chitosan sorbate do not inhibit *B. cinerea* spore germination or growth of *E.coli* colonies. For example, in Example 2, Table 2, that chitosan sorbate and chitosan propionate at a 0.1% concentration do not inhibit *B. cinerea* (there is 0% inhibition of spore germination) or *E.coli.* (there are hundreds of CFU). In Example 3, Table 4, concentrations of chitosan acetate, chitosan propionate, and chitosan sorbate at 0.0016 and 0.0032% did not inhibit at all, *i.e.*, the colony number was too numerous to count. In Example 3, Table 7, concentrations of chitosan acetate at 0.06% (v/v) or less did not inhibit at all; concentrations of chitosan propionate at 0.06% (v/v) or less did not inhibit at all; and concentrations of chitosan sorbate at 0.015 % (v/v) did not inhibit at all, *i.e.*, spore germination occurred in the presence of those concentrations. Table 10 shows that apples treated with 0.1% concentrations of chitosan sorbate and chitosan propionate, either before or after exposure to *E. coli* cultures, do not inhibit growth of *E. coli* colonies.

Similarly, with regard to the recitation that "the concentration of the essential oil is in the range of 0.025 - 0.1% (v/v)." Table 5 discloses savory, thyme red, and carvacol at concentrations of 0.025% (v/v), cinnamon, at 0.050% (v/v), and bay, allspice, birch, cloves, and hinokitiol at 0.075% (v/v). As shown in Table 3, savory, thyme red, and carvacol do not inhibit at all at concentrations of 0.025% (v/v). Table 3 also shows that cinnamon does not inhibit at all at concentrations of 0.050% (v/v) or lower and that bay, allspice, birch, cloves, and hinokitiol do not inhibit at all at concentrations of 0.075% (v/v) or lower. Table 2 shows that cinnamon, savory, and allspice do not inhibit growth of E. coli colonies at all when used at a concentration of 0.1% (v/v).

Therefore, Table 5 shows that examples of chitosan salts: chitosan acetate, chitosan proprionate, and chitosan sorbate, when used at a concentration that is not inhibitory at all, *i.e.*, 0.0032% (v/v) (as shown in Table 4) together with essential oils at concentrations that are not inhibitory at all (as shown in Table 3) act synergistically to inhibit growth of *E. coli* colonies. Similar results were observed when spore germination of *B. cinerea* was measured after determining appropriate low concentrations by a similar strategy; see Tables 6, 7, and 8.

Thus, the composition of Applicant comprises concentrations of essential oils and chitosan that absolutely do not inhibit by themselves, but inhibit totally or substantially when combined, *i.e.*, they act synergistically. Combining two substances in non-inhibitory concentrations, unexpectedly results in a synergistic response as discussed in the above examples.

Finally, with regard to the Examiner's statement that states "'[P]referably', like the phrase 'such as' can be treated as an alternative recitation. That is , 'A preferably B

can b construed as just A'", Applicant has amended Claim 21; "preferably" has been deleted from the claim.

In view of the amendment and the above remarks, it is respectfully requested that the rejection of Claims 3-21 under 35 U.S.C. 112, first paragraph, be withdrawn.

Rejection of Claims* 3, 6-9, 14 and 15 *under 35 U.S.C.103(a)

6. The Examiner has rejected Claims 3-21 under 35 U.S.C. 103(a) as being unpatentable over Takahashi (U.S. Patent 6,352,727, 2002) in view of Ozawa (JP 10-195,766), Atsumi *et al.* (JP 200217509), and Packpia (1996, Vol. 40, No. 1, pages 132-138).

The Examiner states that the phrase "not inhibitory in the absence of the other" "does not appear to be clearly defined as noted above" ("above" referring to the rejection under 35 U.S.C. 112, first paragraph of the paper of June 16, 2004, Page 2) and that "in any case, it is not clear whether the concentrations of the chitosan salt (or chitosan) and the essential oil in Takahashi inherently meet this concentration or not". The Examiner continues, "since it is not clear, the rejection is made under obviousness, 35 U.S.C. 103" (Paper of June 16, 2004, Page 3).

Applicant respectfully traverses the rejection. Applicant respectfully disagrees with the Examiner's assertion that a *prima facie* case of obviousness has been established. It is stated in the MPEP (MPEP 706.02(j) that "[T]o establish a *prima facie* case of obviousness three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available

to one of ordinary skill in the art, to modify the references to combine reference teachings. Second, there must be reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure."

"The prior art reference (or references when combined) must teach or suggest all the claim limitations." Claim 21 recites a composition which has protectant and/or eradicant activity and which substantially inhibits bacterial and fungal growth, comprising a chitosan salt and an essential oil in a synergistically effective amount wherein the chitosan salt is present in an amount which is not inhibitory in the absence of the essential oil, wherein the concentration of the chitosan salt is in the range of 0.0016 - 0.1% (v/v), and wherein the essential oil is present in an amount which is not inhibitory in the absence of the chitosan salt, wherein the concentration of the essential oil is in the range of 0.025 - 0.1% (v/v). The references cited by the Examiner do not teach or suggest all claim limitations.

As Applicant has stated above, "to clarify, the phrase 'not inhibitory' means that a particular concentration of the component has no antibacterial or antifungal ability at all, *i.e.*, there is 0% inhibition or colony growth is not inhibited." In Applicant's response above to the rejection under 35 U.S.C. 112, first paragraph, Applicant has pointed to support in the specification: "the specification teaches that particular concentrations of chitosan acetate, chitosan propionate, and chitosan sorbate do not inhibit *B. cinerea* spore germination or growth of *E.coli* colonies. For example, in Example 2, Table 2, that chitosan sorbate and chitosan propionate at a 0.1% concentration do not inhibit *B.*

cinerea (there is 0% inhibition of spore germination) or *E.coli.* (there are hundreds of CFU). In Example 3, Table 4, concentrations of chitosan acetate, chitosan propionate, and chitosan sorbate at 0.0016 and 0.0032% did not inhibit at all, *i.e.*, the colony number was too numerous to count. In Example 3, Table 7, concentrations of chitosan acetate at 0.06% (v/v) or less did not inhibit at all; concentrations of chitosan propionate at 0.06% (v/v) or less did not inhibit at all; and concentrations of chitosan sorbate at 0.015 % (v/v) did not inhibit at all, *i.e.*, spore germination occurred in the presence of those concentrations. Table 10 shows that apples treated with 0.1% concentrations of chitosan sorbate and chitosan propionate, either before or after exposure to *E. coli* cultures, do not inhibit growth of *E. coli* colonies.

Similarly, with regard to the recitation that "the concentration of the essential oil is in the range of 0.025 - 0.1% (v/v)." Table 5 discloses savory, thyme red, and carvacol at concentrations of 0.025% (v/v), cinnamon, at 0.050% (v/v), and bay, allspice, birch, cloves, and hinokitiol at 0.075% (v/v). As shown in Table 3, savory, thyme red, and carvacol do not inhibit at all at concentrations of 0.025% (v/v). Table 3 also shows that cinnamon does not inhibit at all at concentrations of 0.050% (v/v) or lower and that bay, allspice, birch, cloves, and hinokitiol do not inhibit at all at concentrations of 0.075% (v/v) or lower. Table 2 shows that cinnamon, savory, and allspice do not inhibit growth of E. coli colonies at all when used at a concentration of 0.1% (v/v).

Therefore, Table 5 shows that examples of chitosan salts: chitosan acetate, chitosan proprionate, and chitosan sorbate, when used at a concentration that is not inhibitory at all, *i.e.*, 0.0032% (v/v) (as shown in Table 4) together with essential oils at concentrations that are not inhibitory at all (as shown in Table 3) act synergistically to inhibit growth of *E. coli* colonies. Similar results were observed when spore germination

of *B. cinerea* was measured after determining appropriate low concentrations by a similar strategy; see Tables 6, 7, and 8.

Thus, the composition of Applicant comprises concentrations of essential oils and chitosan that absolutely do not inhibit by themselves, but inhibit totally or substantially when combined, *i.e.*, they act synergistically. Combining two substances in non-inhibitory concentrations, unexpectedly results in a synergistic response as discussed in the above examples".

There is nothing in Takahashi which teaches the limitations (concentrations and conditions) of the instant claims and the concentrations of the chitosan salt (or chitosan) and the essential oil in Takahashi do not inherently meet the concentrations and conditions of the claims.

7. The Examiner alleges that "since Takahashi discloses that the combination of either chitosan or chitosan salts and essential oils provide synergistic antibacterial and anti-fungal properties, the selection of the particular concentrations of the components to provide a synergistic result would have been obvious routine determination, fairly led by the teachings of the art. Ozawa et al. can be relied on as further evidence that it was well established in the art to combine chitosan salts and an essential oil (e.g. hinokitiol) for their antibacterial function. Atsumi et al is also relied on as further evidence of chitosan/essential oil anti-bacterial combinations" (Office Action, June 16, 2004, Pages 3-4).

Applicant respectfully traverses the rejection. Applicant respectfully disagrees with the Examiner's assertion that the selection of the particular concentrations of the components to provide a synergistic result would have been obvious routine

determination. The Examiner has provided no evidence that Takahashi or Ozawa *et al.* or Atsumi *et al.* would utilize the concentrations of the instant invention to obtain a synergistic combination. While Takahashi uses the word "synergic", he is not using the word "synergic" as "synergistic" is commonly used in the art. In fact, the word "synergic" is defined as "working together, co-operating" in Webster's English Dictionary. The specification of Takahashi discloses a combination wherein the effects of the individual components are "additive" in contrast to the "synergistic" effects of the instant invention. There is nothing the teachings of Ozawa *et al.* or Atsumi *et al.* which overcomes the deficiencies of the Takahashi reference.

In contrast, the instant specification discloses "[A]s used herein, the term "synergism" is intended to include both an increased spectrum of activity (*i.e.*, greater activity against a broad spectrum of microorganisms), and/or increased efficacy (*i.e.*, greater activity against specific organisms than that predicted by use of either agent alone). The increased antimicrobial and antifungal activity of the synergistic combination permits the use of smaller amounts of each agent thereby decreasing costs and minimizing other problems, *e.g.*, toxicity, solubility, availability. Effectiveness against a broad spectrum of microorganisms broadens the utility of the synergistic product based on its effectiveness in environments containing many and diverse microorganisms which must be controlled" (Page 6). The composition of Atsumi *et al.* comprises concentrations of hinokitiol and chitosan that inhibit when used alone, although not very well. The combination of a somewhat inhibitory concentration of hinokitiol and a somewhat inhibitory concentration of chitosan results in somewhat better inhibition, which Atsumi *et al.* consider a synergistic effect (Paragraph 21). However, in the art, such results would be considered little more than additive. The composition of Applicant, however, comprises concentrations of essential oils and chitosan that absolutely do not inhibit by themselves, but inhibit totally or substantially when combined, *i.e.*, they act

synergistically. Combining two substances in non-inhibitory concentrations, unexpectedly results in a synergistic response. See, for example, Tables 6 and 8, Pages 18 and 19.

Thus, the prior art reference (or references when combined) do not teach or suggest all the claim limitations.

8. Therefore, taking the following facts into account: (1) the absence in Takahashi, Ozawa *et al.*, or Atsumi *et al.* of a teaching of a composition which has protectant and/or eradicant activity and which substantially inhibits bacterial and fungal growth, comprising a chitosan salt and an essential oil in a synergistically effective amount wherein the chitosan salt is present in an amount which is not inhibitory in the absence of the essential oil, wherein the concentration of the chitosan salt is in the range of 0.0016 - 0.1% (v/v), and wherein the essential oil is present in an amount which is not inhibitory in the absence of the chitosan salt, wherein the concentration of the essential oil is in the range of 0.025 - 0.1% (v/v), (2) the lack of a teaching of the motivation to combine the references and (3) the absence of a reasonable expectation of success to obtain particular synergistic combinations and concentrations, it would not have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have obtained the claimed invention.

In view of the above, it is respectfully requested that the rejection of Claims 3-21 under 35 U.S.C. paragraph 103 be withdrawn.

CONCLUSION

Please charge any additional fees which may be required at any time during prosecution of the instant application to deposit account 50-2134.

In view of the above amendments and remarks, it is believed that all of the claims and the specification are in condition for allowance. Accordingly, it is respectfully requested that the rejections be withdrawn and that the instant application be allowed to issue. If any issues remain to be resolved, the Examiner is invited to telephone the undersigned at the number below.

Respectfully submitted,

December 16, 2004 Evelyn M. Rabin

Date

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